

CLAIMS

1. A minus-strand RNA virus carrying a foreign gene, wherein the wild type of the foreign gene comprises in its sense strand sequence a part of an antigenome E sequence of the minus-strand RNA virus, and wherein the foreign gene has been altered at the part of the E sequence to lower the identity with the E sequence.
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2. A minus-strand RNA virus carrying a foreign gene, wherein the foreign gene has been altered at the 5'-AGA₅₋₆C-3' sequence comprised in the sense strand of the wild type of the foreign gene.
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3. The minus-strand RNA virus of claim 2, wherein the 5'-AGA₅₋₆C-3' sequence is present in the protein-encoding sequence of the wild-type gene, and the foreign gene has been altered at the 5'-AGA₅₋₆C-3' sequence such that the amino acid sequence encoded by the 5'-AGA₅₋₆C-3' sequence of the wild-type gene is maintained.
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4. The minus-strand RNA virus of claim 2, wherein the 5'-AGA₅₋₆C-3' sequence is part of a 5'-AGA₅₋₆CTT-3' sequence.
- 20 5. The minus-strand RNA virus of claim 2, wherein the foreign gene is the human CFTR gene.
6. The minus-strand RNA virus of claim 1 or 2, wherein the minus-strand RNA virus is a paramyxovirus.
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7. The minus-strand RNA virus of claim 1 or 2, wherein the minus-strand RNA virus is a Sendai virus.
8. A DNA encoding the genome RNA of the minus-strand RNA virus of claim 1 or 2, or
30 a complementary strand thereof.
9. A method for producing a minus-strand RNA virus carrying a gene which is altered to lower mutation frequency, wherein the gene before alteration comprises in its sense strand sequence a part of an antigenome E sequence of the minus-strand RNA virus, and wherein the method comprises the steps of:
35 (a) altering the part of the E sequence in the sense strand sequence to a different sequence to

lower identity to the E sequence;

(b) preparing a DNA encoding the genome of the minus-strand RNA virus into which the altered gene has been inserted, or a complementary strand thereof; and

(c) reconstituting the minus-strand RNA virus by transcribing the DNA.

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10. A method for producing a minus-strand RNA virus carrying a gene which is altered to lower mutation frequency, wherein the gene sequence before alteration comprises a 5'-AGA₅₋₆C-3' sequence, and wherein the method comprises the steps of:

(a) altering the 5'-AGA₅₋₆C-3' sequence;

10 (b) preparing a DNA encoding the genome of the minus-strand RNA virus into which the altered gene has been inserted, or a complementary strand thereof; and

(c) reconstituting the minus-strand RNA virus by transcribing the DNA.

11. The method of claim 10, wherein the 5'-AGA₅₋₆C-3' sequence is part of a
15 5'-AGA₅₋₆CTT-3' sequence.

12. The method of claim 10, wherein the gene is a human CFTR gene.

13. The method of claim 9 or 10, wherein the minus-strand RNA virus is a
20 paramyxovirus.

() 14. The method of claim 9 or 10, wherein the minus-strand RNA virus is a Sendai virus.